

# INPLASY PROTOCOL

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**Conflicts of interest:**  
None declared.

## Quality of Evidence Supporting the Role of Nonsteroidal Anti-inflammatory Drugs for the Treatment of Anxious Depression: A protocol for Systematic Review and Meta-analysis

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**Review question / Objective:** Population: the participants had anxious depression diagnosed according to any authoritative diagnostic criteria, no restrictions on sex, race, age, onset time, or the source of cases. Intervention: Nonsteroidal Anti-inflammatory Drugs (NSAIDs), including oral and injectable NSAIDs. Comparison: conventional antidepressants. Outcome: effective rate, Hamilton Depression Rating Scale, Hamilton Anxiety Rating Scale, Treatment Emergent Symptom Scale, potential gastrointestinal and neurological adverse events, etc. Study design: Randomized controlled trial.

**Information sources:** Literature searches were conducted in the Cochrane Library, PubMed, Web of Science, EMBASE, China National Knowledge Infrastructure (CNKI), SinoMed, Chongqing VIP. Gray literature including conference proceedings, fund application report by hand, and other possible sources including citation searching and websites.

**INPLASY registration number:** This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 08 August 2022 and was last updated on 08 August 2022 (registration number INPLASY202280029).

### INTRODUCTION

**Review question / Objective:** Population: the participants had anxious depression diagnosed according to any authoritative diagnostic criteria, no restrictions on sex, race, age, onset time, or the source of

cases. Intervention: Nonsteroidal Anti-inflammatory Drugs (NSAIDs), including oral and injectable NSAIDs. Comparison: conventional antidepressants. Outcome: effective rate, Hamilton Depression Rating Scale, Hamilton Anxiety Rating Scale, Treatment Emergent Symptom Scale,

potential gastrointestinal and neurological adverse events, etc. Study design: Randomized controlled trial.

**Rationale:** An objective description is used in this overview. The characteristics and results of each SR/MA and the evaluation results of Assessing the Methodological Quality of Systematic Reviews 2, Risk of Bias in Systematic reviews, Preferred Reporting Items for Systematic Reviews and Meta-Analyses, and Grading of Recommendations, Assessment, Development and Evaluation are reported in the form of a list.

**Condition being studied:** Major depressive disorder (MDD) is one of the most common clinical psychiatric disorders. It is a type of mood disorder characterized by significant and persistent depression from various causes, with a lifetime prevalence of about 16%. In addition to common physical comorbidities, patients with depression often have co-occurring anxiety disorder (AD). According to the DSM-5 (Diagnostic and Statistical Manual of Mental Disorders, 5th Edition) criteria, it uses "with anxiety distress descriptor" in its MDD section to define anxious depression. Epidemiological studies and clinical research have found that approximately 60-90% of patients with MDD have co-occurring anxiety symptoms or co-occurring anxiety disorders, which typically result in more severe functional impairment, greater antidepressant resistance, higher risk of suicide and disability, and lower quality of life for patients with MDD, complicating the treatment process and worsening clinical outcomes.

## METHODS

### Search strategy:

#1

"Depressive disorder"[Mesh] OR "Depressive Symptom"[Title/Abstract] OR "Emotional Depression"[Title/Abstract] OR "Major depressive disorder"[Title/Abstract]

#2

"Anxiety Disorders"[Mesh] OR "Anxiety Symptom"[Title/Abstract] OR "Anxious"[Title/Abstract]

#3 #1 AND #2

#4,

"Anti-Inflammatory Agents"[Mesh] OR "Nonsteroidal Anti-inflammatory Drug"[Title/Abstract] OR "NSAID\*"[Title/Abstract] OR "Anti-Inflammatory treatment"[Title/Abstract] OR "Anti-Inflammatory treatment therapy"[Title/Abstract] OR "Anti-Inflammatory"[Title/Abstract]

#5

"systematic review"[Title/Abstract] OR "meta-analysis"[Title/Abstract] OR "meta-analysis"[Title/Abstract] OR "systematic review"[PT] OR "Systematic Reviews as Topic"[Mesh] OR "meta-analysis"[pt] OR "Meta-Analysis as Topic"[Mesh]

#6

#3 AND #4 AND #5.

**Participant or population:** The participants had anxious depression diagnosed according to any authoritative diagnostic criteria, no restrictions on sex, race, age, onset time, or the source of cases.

**Intervention:** NSAIDs (including oral and injectable NSAIDs) or NSAIDs combined with conventional antidepressants.

**Comparator:** Conventional antidepressants.

**Study designs to be included:** Randomized controlled trial.

**Eligibility criteria:** The exclusion criteria were as follows: (a) animal studies; (b) overviews, network MAs, and narrative reviews; (c) studies in which the required data were unavailable; (d) Conference abstract.

**Information sources:** Literature searches were conducted in the Cochrane Library, PubMed, Web of Science, EMBASE, China National Knowledge Infrastructure (CNKI), SinoMed, Chongqing VIP. Gray literature including conference proceedings, fund application report by hand, and other possible sources including citation searching and websites.

**Main outcome(s):** effective rate, Hamilton Depression Rating Scale, Hamilton Anxiety

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Rating Scale, Treatment Emergent Symptom Scale, potential gastrointestinal and neurological adverse events, etc.

**Quality assessment / Risk of bias analysis:**

The Assessment System for Evaluating Methodological Quality 2 (AMSTAR-2) scale was used in assessing the methodological quality of the included SRs/MAs. The risk of bias of the included SRs/MAs is assessed by the risk of bias in systematic scale. The list of The Preferred Reporting Items for Systematic Reviews and Meta Analyses was adopted to assess the quality of each included SR/MA report. The Grading of Recommendations, Assessment, Development and Evaluation system was used to assess the quality of the evidence of the included SRs/MAs.

**Strategy of data synthesis:** An objective description was used in this overview. The characteristics and results of each SR/MA and the evaluation results of Assessing the Methodological Quality of Systematic Reviews 2, Risk of Bias in Systematic reviews, Preferred Reporting Items for Systematic Reviews and Meta-Analyses, and Grading of Recommendations, Assessment, Development and Evaluation are reported in the form of a list.

**Subgroup analysis:** Not applicable.

**Sensitivity analysis:** Not applicable.

**Language restriction:** No restriction in language.

**Country(ies) involved:** China.

**Keywords:** nonsteroidal anti-inflammatory drugs, anxious depression, meta-analysis, systematic reviews.

**Contributions of each author:**

Author 1 - Chengda Dong designed the study and draft yhe manuscript.

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Author 2 - Hongshuo Shi screened potential studies and extracted data from the included studies.

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Author 3 - Zhaojun Yan assessed the reviews.

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Author 4 - Jianmin Liu provided guidance on the overview methodology and arbitration on disagreement.

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